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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,092	09/22/2005	Ana Velasco Iglesias	13566.105008	7526

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KING & SPALDING
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036-4003

EXAMINER	
ROBINSON, HOPE A	
ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
07/23/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

usptomailnyc@kslaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/540,092	VELASCO IGLESIAS ET AL.	
	Examiner	Art Unit	
	HOPE A. ROBINSON	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *26 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4,6,7,11-13,16-34,43,44 and 46-52* is/are pending in the application.

4a) Of the above claim(s) *16,17,33 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4,6,7,11-13,18-27,32, 43-44 and 46-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/26/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. Applicant's response to the Office Action mailed November 28, 2007 on March 26, 2008 is acknowledged. The claims have been amended to add SEQ ID NO:2-15 and 27-30, applicant is reminded that the claimed invention elected is the nucleic acid (SEQ ID NO:1).

Claim Disposition

2. Claims 46-52 have been added. Claims 2, 4, 6-7, 11-13, 16-34, 43-44 and 46-52 are pending. Claims 2, 4, 6-7, 11-13, 18-27, 32, 43-44 and 46-52 are under examination.

New-Specification Objection

3. The specification is objected to because of the following informalities:

The specification is objected to because the newly submitted abstract discloses "SEQ ID 1" which is improper and should instead be "SEQ ID NO:1".

Information Disclosure Statement

4. The Information Disclosure Statement filed on March 26, 2008 has been received and entered. The references cited on the PTO-1449 Form have been considered by the examiner and a copy is attached to the instant Office action.

5. The following Objections/Rejections are or remain applicable.

New-Claim Objections

6. Claim 2 is objected to because of the following informalities:

For clarity it is suggested that claim 2 is amended to recite "a) the nucleic acid sequence of SEQ IDNO:1"; c) The nucleic acid encoding…" and (e). The nucleic acid sequence…at least 95% sequence identity…".

Maintained and Amended-Claim Rejections - 35 USC ə 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 2, 4, 6-7, 11-13, 18-27, 32, 43-44 and 46-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification is not enabled for the full scope of

the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The enablement requirement refers to the requirement that the specification describe how to make and how to use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: Quantity of Experimentation Necessary; Amount of direction or guidance presented; Presence or absence of working examples; Nature of the Invention; State of the prior art and Relative skill of those in the art; Predictability or unpredictability of the art and Breadth of the claims (see *In re Wands, 858 F.2d at 737, 8 USPQ2d at1404 (Fed. Cir. 1988*). The factors most relevant to the instant invention are discussed below.

The claimed invention is directed to “a nucleic acid” and “a contiguous portion of SEQ ID NO:1. In addition, the claims recite the open language "comprising", thus the claims encompass a large variable genus of variants/derivatives based on the aforementioned language. Additionally, the claims are directed to a probe subjected to stringent hybridization conditions, however, no conditions are provided in the instant claims. Due to the large quantity of experimentation necessary to generate the infinite number of variants/derivatives recited in the claims and possibly screen same for activity and the lack of guidance/direction provided in the instant specification, this is merely an invitation to the skilled artisan to use the current invention as a starting point for further experimentation. Thus, undue experimentation would be required for a skilled

artisan to make and/or use the claimed invention commensurate in scope with the claims.

Moreover, neither the claims nor the instant specification identifies conserved regions/domains for the variants or where in the sequences modifications can occur or what modifications can be tolerated by the claimed structures. Note that claims such as claim 2 recites "a contiguous portion of SEQ ID NO:1" reads on any fragment or variant of the disclosed SEQ ID NO:1 which has 26705 nucleotides. Therefore, no correlation has been made been structure and function. Thus, absent adequate guidance/direction one of skill in the art would not be able to practice the claimed invention commensurate in scope with the claims based on the disclosure in the art which renders the claimed invention as unpredictable. Therefore, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

With regard to the recited "portion of SEQ ID NO:1", this renders the claimed invention as unpredictability because there is no indication of which potential changes can be tolerated to result in an encoded protein that has function. The state of the prior art provides evidence for the high degree of unpredictability as stated above. Seffernick et al. (J. Bacteriology, vol. 183, pages 2405-2410, 2001) disclose two polypeptides having 98% sequence identity and 99% sequence identity, differing at only 9 out of 475 amino acids (page 2407, right column, middle and page 2408, Fig. 3). The polypeptides of Seffernick et al. are identical along relatively long stretches of their respective sequences (page 2408, Fig. 3), however, these polypeptides exhibit distinct functions.

The modifications exemplified in the Seffernick et al. reference is small compared to those contemplated and encompassed by the claimed invention.

The specification lacks adequate guidance/direction to enable a skilled artisan to practice the claimed invention commensurate in scope with the claims. Furthermore, while recombinant and mutagenesis techniques are known in the art, it is not routine in the art to screen large numbers of mutated proteins where the expectation of obtaining similar activity is unpredictable based on the instant disclosure. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what mutations can be tolerated in a protein's sequence and result in certain activity, which is very complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's function from mere sequence data are limited, therefore, the general knowledge and skill in the art is not sufficient, thus the specification needs to provide an enabling disclosure.

The working examples provided do not rectify the missing information in the instant specification pertaining to the claimed variant. The nature and properties of this claim is difficult to ascertain from the examples provided as one of skill in the art would have to engage in undue experimentation to construct the variants encompassed in the claims and to examine the same for function.

The specification does not provide support for the broad scope of the claims, which encompass an unspecified amount of variants/fragments of the claimed nucleic acid. The claims broadly read on any portion thereof. The issue in this case is the breath of the claims in light of the predictability of the art as determined by the number

of working examples, the skill level artisan and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)* where it is stated that "...scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)*.

Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of guidance and working examples provided in the specification and the high degree of unpredictability as evidenced by the state of the prior art, attempting to construct and test derivatives of the claimed invention would constitute undue experimentation. Making and testing the infinite number of possible variants to find one that functions as described is undue experimentation. Therefore, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

8. Claims 2, 4, 6-7, 11-13, 18-27, 32, 4344 and 46-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is directed to a nucleic acid or a contiguous portion of SEQ ID NO:1. In addition, the claims recite “stringent hybridization” absent specific hybridization conditions. The claims are directed to a genus of nucleic acids and proteins that are not adequately described as a skilled artisan cannot envision the detailed chemical structure of the derivatives encompassed in the claims. The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials'. University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

The specification fails to provide any additional representative species of the claimed genus to show that applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described, are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Further, no relationship between the disclosed species and the structures of the other proposed species is described. Thus, one of skill in the art would be unable to predict the structure of other members of this genus based on the instant disclosure. Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Further, *Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991)*, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. *See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993).*

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 11-13 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter, which applicant (s) regard as their invention.

Claims 11-13 remain indefinite for the recitation of "stringent conditions" absent specific hybridization conditions because it is unclear what values to equate with that terminology since the art recognizes that hybridization conditions can vary, especially the wash conditions. Thus, the metes and bounds is unclear.

Maintained-Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 2, 4,6-7, 18-22, 24-27, 32 and 43-44 remain rejected under 35 U.S.C. 102(b) as being anticipated by Pospiech et al. (Microbiology, vol. 141, pages 1793-1803, February 18, 1999) based on the broad recitation of variant or portion thereof.

Pospiech et al. teach a gene cluster derived from *Myxococcus Xanthus* DM504/15. The reference teaches that tagged genes were cloned and used to select overlapping cosmids. These genes were sequenced and a region encodes two amino acid domains with similarity to peptide synthetase (a non-ribosomal multienzyme complex). The reference sequence is a portion or variant thereof for the claimed SEQ ID NO:1 and thus is homologous to SEQ ID NO:2. The reference teaches the use of plasmids and the transformation of *E. coli* with the expression vector. The reference also teaches gene disruption experiments (see pages 1793 and 1796 of the reference). Therefore, the limitations of the claims are met by the reference.

Response to Applicant's Arguments:

11. The response has been considered in full, however is not persuasive. Note that rejections under 35 U.S.C. 112 first and second paragraph and 102(b) remains. Applicant state that the enablement rejection is traversed based on the amendments made to the claims, for example it is stated that claim 2 specifies SEQ ID NO:1. This argument is not persuasive. First claim 1 recites "a portion of the nucleic acid in item (d) and the claim is directed to "a nucleic" which encompasses variants and fragments as the claim is not claiming "the" specific one (see the objections made to the claim language above). Applicant argues that the claims present a structure function relationship. This argument is not persuasive because there is no indication in the claims for example, of what portion of the DNA is referred to and the claims also recite, “comprising a nucleic acid” which encompasses an enormous amount of fragment/variants for a sequence that has 29705 nucleotides.
.Applicants state that the claims are amended to read “95% homology, however, homology refers to evolutionary ties, thus the claims should be amended to recited 95% sequence identity which speaks to the comparison or alignment of the claimed sequence with another.

With regard to the written description rejection applicants state that the claims have been amended. However, the amendments made did not obviate this ground of rejection. As stated above the claims are still drawn to a genus of nucleic acids, thus a genus of encoded proteins. Note that the “portion thereof “language remains as well as the hybridization language without specific conditions. As the claims were not amended to specifically recite the conditions that are stringent, the rejection under 112 second paragraph remains. Applicants state that conditions will vary based on the GC content,

hence the reason the skilled artisan needs to be provided with guidance as to what the conditions are for the claimed invention. The claims remains indefinite because no conditions are defined and based on the variability known in the art and admitted by applicants, the metes and bounds of the claims are undefined.

Applicants state that the art rejection should be withdrawn based on the amendments to the claims. However, the amendments made were not sufficient to obviate this ground of rejection. The claims still read broadly on any fragment or variant thereof. Thus the rejections of record remain.

OIPE will be contacted by the examiner to resolve the issue raised by applicant.

Conclusion

12. No claims are allowable.

13. Applicant's amendment necessitated the new/modified ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed, can be reached at (571) 272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Hope A. Robinson/

Primary Examiner, Art Unit 1652